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10/081,327	02/21/2002	Tim Hui-Ming Huang	40629-2	3584

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EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

4C

Office Action Summary	Application No.	Applicant(s)	
	10/081,327	HUANG, TIM HUI-MING	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-80* is/are pending in the application.

4a) Of the above claim(s) *18-80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed February 10, 2005. Currently, claims 1-80 are pending. Claims 18-80 have been withdrawn as drawn to non-elected subject matter.

Election/Restrictions

2. Applicant's election of Group I, Claims 1-17 and SEQ ID NO: 36 in the paper filed February 10, 2005 is acknowledged. Applicant relies upon the arguments already of record in the underlying US Parent application.

Claims 18-80 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

The requirement is still deemed proper and is therefore made FINAL.

This application contains claims 18-80 drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

3. This application claims priority to 09/497,855, filed February 4, 2000, Provisional Applications 60/118,760 filed 5 February 1999 and 60/120,592 18 February 1999. The provisional applications provide adequate support under 35 U.S.C. 112 for claims 1-16 of this application. However, the Provisional Applications do not provide adequate support for Claim 17.

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Drawings

4. The drawings are acceptable.

Claim Objections

5. Claims 1-17 are objected to because of the following informalities: The method steps of Claim 1 are labeled "a." through "g." each label having an improper "." (period). It is required that Claim 1 be amended to delete the "." In steps "a." through "g.".

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-17 are indefinite in Claim 1 for the recitations "linker primer products" and "linker products" because "products" lacks proper antecedent basis in the

"fragments" of step "a." It is suggested that Claim 1 be amended to replace "products" with "fragments" and to replace "linker products" with "linker primer fragments".

B) Claims 1-17 are indefinite because Claim 1 is drawn to a process for detecting the presence or absence of methylation of a CpG dinucleotide rich region, but the claim does not recite a step of detecting the claimed CpG dinucleotide rich region. It is suggested that Claim 1 be amended to clarify e.g. recite at the end of Claim 1 "to thereby detect the presence or absence of methylation of a CpG dinucleotide rich region".

C) Claims 3-9 are indefinite in Claim 3 for the recitation "nucleic acid fragments" because the recitation lacks proper antecedent basis in the "plurality of nucleic acid fragments" of Claim 1. It is suggested that Claim 3 be amended to provide proper antecedent basis i.e. insert "plurality" before "nucleic acid".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duffy (U.S. Patent No. 5,871,917, filed 31 May 1996), Sapolsky et al. (U.S. Patent No. 6,027,894, filed 16 January 1998), Cross et al. (Nature Genetics, March 1994 6: 236-244) and Pirrung et al. (U.S. Patent No. 5,143,854, filed 7 March 1990).

Regarding Claim 1, Duffy teaches a process for detecting the presence or absence of methylation of a CpG dinucleotide rich region of a nucleic acid sequence within a genome, the process comprising: contacting the nucleic acid sequence with an enzyme (i.e. MseI) which digests the nucleic acid sequences into fragments in which CpG islands are preserved (Column 21, lines 55-60); attaching the fragments to linker primers to form linker primer products (Column 21, lines 61-63); contacting the linker primer products with a methylation-sensitive enzyme (i.e. MspI) which digests the linker products having unmethylated CpG dinucleotides sequences but not methylated CpG dinucleotide sequences to form a digestion product comprising methylated CpG island loci (Column 22, lines 35-37); amplifying the digestion product to form amplicons; (Column 23) and determining the presence or absence of amplicons (Column 24, lines 24-60) wherein the presence or absence is determined by Southern blotting. The additional steps of Duffy are encompassed by the open claim language "comprising"

recited in the instant claims. Duffy does not teach labeling of the amplicons or contacting the amplicons with a screening array. However, Sapolsky et al. teach a similar method for detecting the presence of a nucleic acid sequence within a genome comprising: contacting the nucleic acid sequence with an enzyme; amplifying the digestion product; labeling the amplified product; contacting the labeled product with a screening array comprising a plurality of nucleic acid fragments affixed to a solid support; and determining the presence of the amplified product (Column 4, lines 21-44 and Example 2). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify Southern blotting detection of Duffy with the labeled amplification product detection on a screening array as taught by Sapolsky et al. for the expected benefit of screening large numbers of sequence-specific genomic regions rapidly as taught by Sapolsky et al. (Column 2, lines 4-13). Additionally, It would have been obvious to one of ordinary skill in the art to modify the method of Duffy by omitting the additional amplification and ligation steps for the obvious benefit of detecting the presence of methylated CpG sequences with economy of time and labor. The courts have stated that it would be obvious to omit an element when a function attributed to said element is not desired or required (see Ex parte Wu, 10 USPQ 2031).

Regarding Claim 2, Sapolsky et al. teach the nucleic acid fragments are derived from a genomic sequence of interest (Column 3, lines 27-39) but they do not teach the genomic sequences are CpG dinucleotide rich library. However, Cross et al. teach CpG dinucleotide rich library and they teach the library comprises genomic sequences of interest and importance (page 236, left column, paragraphs 1-2). It would have been

obvious to one of ordinary skill in the art at the time the claimed invention was made to modify further modify the screening of Duffy by modifying the genomic sequences of interest in the screening array of Sapolsky et al. with the CpG dinucleotide rich library taught by Cross et al. for the expected benefit of screening for genomic sequences and markers of importance as taught by Cross et al. (page 236, left column, second paragraph, lines 8-14).

Regarding Claim 3, Cross et al. teach the nucleic acid fragments comprise at least about 200 nucleotides (page 237, left column, last paragraph, lines 6-8) of which at least about 50% are guanine and cytosine (page 239, left column, last paragraph-right column and Fig. 6).

Regarding Claim 4, Sapolsky et al. teach the screening array wherein at least 20 nucleic acid fragments are affixed i.e. one block of probes comprises 40 probes (Column 10, lines 25-45).

Regarding Claim 5, Cross et al. teach the fragments comprise the 5' end of the gene (page 241, left column, first paragraph, lines 1-2) but they do not specifically teach the fragments each containing a promoter and first exon. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made that the promoter and first exon of a gene taught by Cross et al. are located at the 5' end of the gene.

Regarding Claim 6, Cross et al. teach the fragments comprise the 5' end of the gene (page 241, left column, first paragraph, lines 1-2) but they do not specifically teach the sequence is expressed in an organism. However, it would have been obvious to one

of ordinary skill in the art at the time the claimed invention was made that the sequences expressed in an organism comprise the 5' end of a gene. Therefore, the sequence taught by Cross et al. (i.e. 5' end of the gene) inherently comprise an expressed sequence.

Regarding Claim 7, Sapolsky et al. teach the screening array wherein at least 20 nucleic acid fragments are affixed i.e. one block of probes comprises 40 probes (Column 10, lines 25-45).

Regarding Claims 8-9, Sapolsky et al. teach the screening array wherein at least 100 nucleic acid fragments (Claim 8) and at least 500 nucleic acid fragments (Claim 9) are affixed i.e. one block of probes comprises 40 probes and the screening array comprises 50 to 4000 detection blocks (Column 6, lines 26-34).

Regarding Claim 10, Sapolsky et al. teach the solid support of the screening array comprises glass or silicon (Column 3, lines 40-46) by incorporation of the teaching of Pirrung et al. who teach the solid support comprises glass or silicon (Column 11, lines 51-57)

Regarding Claim 11, Sapolsky et al. teach the label is fluorescent (Column 10, lines 54-57).

Regarding Claim 12, Duffy teaches the process wherein the enzyme is MseI and the methylation sensitive enzyme is MspI (Column 21, lines 55-57 and Column 22, lines 35-37).

Regarding Claim 13, Duffy teaches the process wherein the enzyme is MseI and the methylation sensitive enzyme is MspI (Column 21, lines 55-57 and Column 22, lines

35-37) but they do not teach the methylation sensitive enzyme is BstUI. However, BstUI was known in the art at the time the claimed invention was made and it would have been obvious to one skilled in the art to modify the MspI of Duffy with BstUI based on equal methylation sensitivity and based on available reagents for the obvious benefit of economy of reagents.

Regarding Claim 14, Duffy teaches the method wherein the nucleic acid sequence comprises a nucleic acid sequence isolated from a cancer cell (Claim 32).

Regarding Claim 15, Duffy teaches the method wherein the cancer cell is selected form the group consisting of breast cancer, colon cancer, liver cancer and ovarian cancer (Claim 32).

Regarding Claim 16, Duffy teaches the method wherein the cancer cell is breast cancer (Claim 32).

11. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Donini et al. Genome, 1997, 40: 521-526), Sapolsky et al. (U.S. Patent No. 6,027,894, filed 16 January 1998), Cross et al. (Nature Genetics, March 1994 6: 236-244) and Pirrung et al. (U.S. Patent No. 5,143,854, filed 7 March 1990)

Regarding Claim 1, Donini et al. teach a process for detecting the presence or absence of methylation of a CpG dinucleotide rich region of a nucleic acid sequence within a genome, the process comprising: contacting the nucleic acid sequence with an enzyme (i.e. Mse) which digests the nucleic acid sequences into fragments in which CpG islands are preserved; attaching the fragments to linker primers to form linker

primer products (page 522, left column, third full paragraph); contacting the linker primer products with a methylation-sensitive enzyme (i.e. Sse) which digests the linker products having unmethylated CpG dinucleotides sequences but not methylated CpG dinucleotide sequences to form a digestion product comprising methylated CpG island loci; amplifying the digestion product to form amplicons; labeling the amplicons; and determining the presence or absence of amplicons (page 522, right column, first paragraph) wherein the labeled amplicons are run of a gel for determining the presence or absence of amplicons. The additional steps of Donini et al. are encompassed by the open claim language "comprising". Donini et al. do not teach contacting the amplicons with a screening array. However, Sapolsky et al. teach a similar method for detecting the presence of a nucleic acid sequence within a genome comprising: contacting the nucleic acid sequence with an enzyme; amplifying the digestion product; labeling the amplified product; contacting the labeled product with a screening array comprising a plurality of nucleic acid fragments affixed to a solid support; and determining the presence of the amplified product (Column 4, lines 21-44 and Example 2). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify Southern blotting detection of Donini et al. with the labeled amplification product detection on a screening array as taught by Sapolsky et al. for the expected benefit of screening large numbers of sequence-specific genomic regions rapidly as taught by Sapolsky et al. (Column 2, lines 4-13). Additionally, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Donini et al. by omitting the additional amplification and

ligation steps for the obvious benefit of detecting the presence of methylated CpG sequences with economy of time and labor. The courts have stated that it would be obvious to omit an element when a function attributed to said element is not desired or required (see Ex parte Wu, 10 USPQ 2031).

Regarding Claim 2, Sapolsky et al. teach the nucleic acid fragments are derived from a genomic sequence of interest (Column 3, lines 27-39) but they do not teach the genomic sequences are CpG dinucleotide rich library. However, Cross et al. teach CpG dinucleotide rich library and they teach the library comprises genomic sequences of interest and importance (page 236, left column, paragraphs 1-2). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify further modify the screening of Donini et al. by modifying the genomic sequences of interest in the screening array of Sapolsky et al. with the CpG dinucleotide rich library taught by Cross et al. for the expected benefit of screening for genomic sequences and markers of importance as taught by Cross et al. (page 236, left column, second paragraph, lines 8-14).

Regarding Claim 3, Cross et al. teach the nucleic acid fragments comprise at least about 200 nucleotides (page 237, left column, last paragraph, lines 6-8) of which at least about 50% are guanine and cytosine (page 239, left column, last paragraph-right column and Fig. 6).

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Regarding Claim 6, Cross et al. teach the fragments comprise the 5' end of the gene (page 241, left column, first paragraph, lines 1-2) but they do not specifically teach the sequence is expressed in an organism. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made that the sequences expressed in an organism comprise the 5' end of a gene. Therefore, the sequence taught by Cross et al. (i.e. 5' end of the gene) inherently comprises an expressed sequence.

Regarding Claim 7, Sapolsky et al. teach the screening array wherein at least 20 nucleic acid fragments are affixed i.e. one block of probes comprises 40 probes (Column 10, lines 25-45).

Regarding Claims 8-9, Sapolsky et al. teach the screening array wherein at least 100 nucleic acid fragments (Claim 8) and at least 500 nucleic acid fragments (Claim 9) are affixed i.e. one block of probes comprises 40 probes and the screening array comprises 50 to 4000 detection blocks (Column 6, lines 26-34).

Regarding Claim 10, Sapolsky et al. teach the solid support of the screening array comprises glass or silicon (Column 3, lines 40-46) by incorporation of the teaching

of Pirrung et al. who teach the solid support comprises glass or silicon (Column 11, lines 51-57)

Regarding Claim 11, Sapolsky et al. teach the label is fluorescent (Column 10, lines 54-57).

Regarding Claims 12-13, Donini teach the process wherein the enzyme is MseI and the methylation sensitive enzyme is Sse (page 522, left column, third full paragraph) but they do not teach the methylation sensitive enzyme is BstUI. However, BstUI was known in the art at the time the claimed invention was made and it would have been obvious to one skilled in the art to modify the MspI of Duffy with BstUI based on equal methylation sensitivity and based on available reagents for the obvious benefit of economy of reagents.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-16, 21 of U.S. Patent No. 6,605,432.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentable distinct from each other because Claims 1-17 of the instant application is generic to all that is recited in Claims 1-16, 21 of U.S. Patent No. 6,605,432. That is, Claim 1-16, 21 of 6,605,432 falls entirely within the scope of Claim 1-17, or in other words, Claim 1-17 is anticipated by Claims 1-16, 21 of 6,605,432. Here, claim 1-16, 21 of U.S. Patent No. 6,605,432 recites a method for detecting the presence or absence of methylation of CpG dinucleotide rich regions of nucleic acid sequences by contacting with an enzyme, ligating a linker, digesting with an enzyme, amplifying, labeling, contacting with an array and determining the presence of labeled amplicons.

Conclusion

10. No claims allowable over the art.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is

(571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

J. Goldberg

Jeanine Goldberg
Primary Examiner
March 16, 2005